REMARKS

This document is filed in reply to the Office Action dated February 13, 2006 ("Office Action").

Applicants have amended the specification to insert sequence identifiers and submitted herewith (i) a paper copy and a computer readable copy of a substitute Sequence Listing under 37 CFR §§ 1.823(a) and 1.824, and (ii) a statement under 37 CFR § 1.821(f). Applicants respectfully request entry of the paper copy and computer readable copy of the substitute Sequence Listing. The amendments merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification. No new matter has been added.

At the Examiner's request, Applicants have amended the specification to delete embedded hyperlinks and amended the Abstract. In particular, Applicants have completed "the first 'sentence' of the Abstract" although the original version is in compliance with MPEP. More specifically, MPEP 608.01(b)E provides three sample abstracts. Each of the sample abstracts starts with a phase, instead of a "sentence."

Applicants have amended claim 6 to incorporate a limitation recited in claim 1, to remove non-elected species, and to specify activity of the polypeptide recited in the claim. As suggested by the Examiner, Applicants have amended claims 7 and 22-25 to remove non-elected species; and claims 8-11 and 22-25 to correct informalities. Applicants have also canceled claims 1-5, 18, 19, and 21; and added new claims 26-33. Support for "[a polypeptide] has activity of increasing the sensitivity of a plant to an environmental factor" recited in claim 6 can be found in the specification at page 10, lines 6-7 and page 11, lines 28-30. Support for "isolated nucleic acid" appears in original claim 6. Support for "regenerate a plant" can be found at page 14, line 11 of the specification. Support for new claims 26-27 can be found, e.g., in the specification at page 11, lines 16-20. Support for new claims 28-29 appears in original claims 24-25 and at page 11, lines 23-28 of the specification. Support for new claims 30-33 can be found in original claims 2-5. No new matter has been introduced.

Upon entry of the proposed amendments, claims 6-17, 20, and 22-33 will be pending. Claims 16, 17, and 20 have been withdrawn from further consideration for covering non-elected

inventions. Claims 6-15 and 22-33 are now under examination. Reconsideration of this application is requested in view of the following remarks.

Objections to Specification and Claims

The Examiner objected to the specification and claims 6, 8-12, 14, and 25 on a number of grounds. See the Office Action, page 2, line 14 to page 3, line 20. Applicants have amended the specification and claims as suggested by the Examiner and submitted a substitute sequence listing. It is respectfully requested that the objections be withdrawn.

Rejections under 35 U.S.C. § 101 and § 112, first paragraph

The Examiner rejected claim 25 for lack of utility, stating that "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. " See the Office Action, page 4, lines 6-7.

Applicants disagree. Claim 25 is drawn to a method of producing a transgenic plant. According to the Examiner, the transgenic plant has "increased sensitivity ... to various environmental stresses. ... It is well established in the art that sensitivity of a plant to various environmental stresses can drastically reduce crop productivity. Thus the claimed method ... does not appear to have any use in the real world." See the Office Action, page 4, lines 9-13.

Applicants note that the specification, at page 11, lines 28-30, asserts that

> The ... transgenic plant is more sensitive to environmental factors, such as high salinity, pathogens, and chilling, and therefore can be used as a sensor to detect and monitor small changes in environment, such as soil and air.

Detecting and monitoring small changes in environment is without question a real-world, i.e., substantial use. Likewise, it is a "specific" utility, in contrast with a "general" utility that would be applicable to the "broad class of the invention" (i.e., all transgenic plants). The Revised Interim Utility Guidelines Training Materials at page 29 provide some hypothetical examples of utilities for subject matter that do not qualify as "specific" utilities because they apply to "virtually every member of a very general class of [plants] ..." In contrast to utilities that apply to all plants, the presently asserted utility clearly

cannot be dismissed as "nonspecific."

The Examiner asserted that "the claimed invention is not supported by ... a well established utility." See the Office Action, page 4, lines 6-7.

Applicants would like to point out that, according to MPEP 2107,

> An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

As discussed above, the method of claim 25 can be used to generate transgenic plant that has increased sensitivity to environmental factors, such as high salinity, pathogens, and chilling. In view of this teachings, "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process)." A person of ordinary skill in the art would also appreciate that the utilities of the invention are "specific, substantial, and credible." Accordingly, the method of claim 25 possesses a well-established utility.

The Examiner further rejected claim 25 for lack of enablement, contending that the claim does not meet the utility requirement so one of skill in the art would not know how to use the claimed invention. See the Office Action, page 4, lines 16-19. As set forth above, the claimed invention does possess utilities. Thus, withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 22-25 for indefiniteness. See the Office Action, page 5, lines 1-7. Applicants have amended the claims as suggested by the Examiner. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 6-14 were rejected as lacking written description and enablement. Applicants respectfully traverse each rejection below and discuss independent claims 6 and 7 first.

Enablement

The Examiner rejected claims 6-14 for lack of enablement and concluded that undue experimentation would be required to enable the full scope of the claims. See the Office Action, page 5, lines 16-20.

Independent claim 6, as amended, is directed to isolated nucleic acids encoding polypeptides that (i) have activity of increasing the sensitivity of a plant to an environmental factor and (ii) are at least 70% identical to SEQ ID NO: 9. Amended claim 7 is drawn to isolated nucleic acids that (i) encode polypeptides having the above-mentioned activity and (ii) hybridize to SEQ ID NO: 20 or its complement. The Examiner first stated that the specification "does not reasonably provide enablement for a nucleic acid that encodes for polypeptide at least 70% but less than 100% identical to SEQ ID NO: 9." See the Office Action, page 5, lines 16-19.

Applicants respectfully traverse. Since the specification teaches how to use polypeptides that have this activity, there is no question that the specification enables one skilled in the art to use each of the polypeptides encoded by the claimed nucleic acids. Similarly, the polypeptides encoded by the claimed nucleic acids can be readily made and tested for this activity according to the methods described in the specification or any other methods known in the art. Thus, Applicants submit that the claims amply meet the enablement requirement.

The Examiner asserted that"[t]here is a lack of specific guidance in the specification as to how any nucleic acid encoding for a polypeptide[] that is at least 70% but less than 100% identical to SEQ ID NO: 9 can be used in a method to produce a product with function identical to SEQ ID NO: 9." See the Office Action, page 6, lines 14-19.

To support this assertion, the Examiner cited Guo *et al.,* which discusses the effects of random point mutations in human AAG protein. Some of these mutations inactivate the protein, while others do not. The Examiner noted that "there is a probability factor of 34% that a random amino acid replacement in a given protein will lead to its functional inactivation." He then proceeded to conclude that "[u]ndue experimentation is required" to enable the full scope of the claims. Applicants respectfully traverse.

Applicants agree that it is possible, at least in some cases, to abolish activity of a given protein by mutating a critical residue, as disclosed by the Guo *et al.* reference. However,

Applicants disagree that this fact means that one of ordinary skill cannot make functional analogs of SEQ ID NO: 9 without undue experimentation.

As correctly pointed out by the Examiner, Guo *et al.* teaches that about 34% of the random replacements led to functional inactivation. Presumably, the other about 76% of the replacements had no noticeable effect on the activity of the protein. Thus, one of ordinary skill can expect, based on Guo *et al.*'s teachings, to find about 76% of random substitutions in any given protein to result in mutated proteins with full or nearly full activity. These are far better odds than those at issue in *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988), in which the court said that screening many hybridomas to find the few that fell within the claims was not undue experimentation. The question is not whether it is possible to abolish activity with a point mutation (as the Examiner seemed to believe), but rather whether one of ordinary skill can produce, without undue experimentation, mutants in which the activity is not abolished. Base on Guo *et al.*'s teachings, one would predict that even random substitution of residues in SEQ ID NO: 9 will predictably result in a majority of the mutants' having full or partial activity of increasing the sensitivity of a plant to an environmental factor.

Further, given the information provided in the specification regarding tubby domains, F-box, TUB motifs, and residues conserved in SEQ ID NO: 9/AtTLP9 (see page 17, line 16 to page 18, line 11), one of ordinary skill would know to avoid those conserved domains/residues or make only conservative changes there, thereby making the predictability of success even higher than the 76% reported in Guo *et al.* In addition, mutagenesis techniques are well known in the art and the specification amply teaches assays for testing mutants (see pages 22-25) to find those with the activity of increasing the sensitivity of a plant to an environmental factor as required by the claims.

In view of the above considerations, Applicants submit that claims 6 and 7 meet the enablement requirement.

Claims 8-14 cover vectors and cells containing the nucleic acids of claim 6 or 7, as well as methods of producing polypeptides encoded by the nucleic acids. New claims 26-29 cover transformed plant cells or transgenic plants containing the nucleic acids of claim 6 or 7, as well as related producing methods. New claims 30-33, dependent from claim 6, cover nucleic acids

having sequences encoding polypeptides that have activity of increasing the sensitivity of a plant to an environmental factor and contain amino acid sequences at least 80%, 90%, 95%, 100% identical to SEQ ID NO: 9. For the same reasons set forth above, claims 8-14, as well as new claims 26-33, also meet the enablement requirement.

The Examiner further rejected claims 10, 11, and 14, drawn to host cells having the above-described nucleic acids or to related methods, stating that "[t]he specification does not describe the use of transforming a host cell other than bacterial or plant cells ... Undue experiment by one skilled in the art is required." See the Office Action, page 7, lines 4-9.

Applicants respectfully traverse. Contrary to the Examiner's statement, the specification explicitly describes the use of host cells other than bacterial or plant cells, e.g., yeast cells, insect cells, and mammalian cells. See the specification, page 11, lines 17-18.

Judging from the Examiner's statement, it appears to be his position that the specification does not provide working examples for these non-bacterial or non-plant cells. Applicants would like to point out that, according to MPEP 2164.02, "[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." and "[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." Here, the specification teaches that all of the above-mentioned host cells can be used to produce a polypeptide of this invention by recombinant DNA technology. As recombinant DNA technology is standard and well known in the art (see, e.g., Maniatis *et al.* cited by the Examiner), "one skilled in the art will be able to practice it without an undue amount of experimentation." Thus, claims 10, 11, and 14 meet the enablement requirement.

Written Description

The Examiner further rejected claims 6-14 for lack of written description to show that Applicants were in possession of the claimed invention at the time of filing. See the Office Action, page 7, paragraph 4.

As currently amended, claim 7 covers a genus of nucleic acids that (i) encode polypeptides have activity of increasing the sensitivity of a plant to an environmental factor and (ii) hybridize under high stringency conditions to SEQ ID NO: 20 or its complement.

Applicants submit that claim 7 is highly analogous to the claim presented in Example 9 of the U.S. Patent and Trademark Office's own guidelines on the subject: Synopsis of Application of Written Description Guidelines, www.uspto.gov/web/menu /written.pdf ("Guidelines"). The Example 9 claim is directed to a nucleic acid that hybridizes under highly stringent conditions to the complement of the disclosed reference sequence, wherein the sequence encodes a protein with specific functional properties. The Example 9 specification discloses a single sequence that falls within the genus covered by the claim. Example 9, at page 36 to page 37, line 2, concludes:

> [A] person of [ordinary] skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

By analogy, Applicants submit that one would not expect substantial variation among species encompassed by claim 7, as the highly stringent hybridization conditions recited yield structurally similar DNA sequences. Thus, as is the case in Example 9, since the genus is narrow, one species (i.e., SEQ ID NO: 20) is sufficient to demonstrate possession. Further, as in Example 9, the instant Specification discloses an assay for the requisite function, i.e., to increase the sensitivity of a plant to an environmental factor. See the Specification, pages 23-25. Applicants therefore submit that the Specification provides an adequate written description of the genus of sequence variants encompassed by claim 7.

Claim 6, as amended, is drawn to nucleic acids comprising sequences encoding polypeptides that (i) are at least 70% to SEQ ID NO: 9 and (ii) having the above-mentioned activity.

Amended claim 6 is highly analogous to the claim in Example 14 of the Guidelines. The Example 14 claim is drawn to a genus of polypeptides that (i) are at least a specific percent identity identical to the disclosed reference sequence and (ii) possess a specific functional property. The Example 14 specification discloses a single sequence that falls within the genus covered by the claim. Just as in the Example 14 hypothetical, "[t]here is a single species disclosed, that species being [SEQ ID NO:20]." Furthermore, just as in the Example 14 hypothetical, there is actual reduction to practice of the disclosed species and a method for assessing the activity of increasing the sensitivity of a plant to an environmental factor is provided (see Detailed Description at pages 23-25). Example 14 then provides the following guidance, "[t]he single species disclosed is representative of the genus ... [and o]ne of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus." See page 54, line 20 to page 55, line 2.

Again, by analogy, Applicants submit that one skilled in the art would not expect substantial variation among species covered by claim 6. Thus, it is submitted that claim 6 meets the written description requirement.

Claims 8-14 and new claims 26-33 have been discussed above. For the same reasons set forth in this section, these claims also meet the written description requirement.

In view of the above remarks, Applicants submit that claims 6-14 and new claims 26-33 meet both the written description requirement and the enablement requirement. Withdrawal of the rejections is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

The Examiner rejected claims 6-9, covering the isolated nucleic acid of SEQ ID NO: 20, for being anticipated by GenBank Accession No. AC011623 ("AC011623") under 35 U.S.C. § 102(a). According to the Examiner , AC011623 teaches a sequence containing SEQ ID NO: 20. See the Office Action, page 9, lines 7-9 and lines 14-16. It is his position that AC011623 was published before the nucleic acid was isolated by Applicants.

Applicants disagree. SEQ ID NO: 20 refers to the cDNA sequence of the AtTLP9 gene. This cDNA was isolated and deposited by Applicants in the GenBank, and assigned Accession

No. AF487270 ("AF487270"). See the specification, page 15, Table 1, row 10; and a printout of AF487270 (attached as "Exhibit A"). As shown in Exhibit A, the cDNA was deposited on Feb. 25, 2002. It follows that the cDNA must have been isolated no later than Feb. 25, 2002. On the other hand, AC011623 cited by the Examiner was published on Oct. 30, 2002, which is after Feb. 25, 2002 and after the invention by Applicants. Accordingly, AC011623 does not qualify as prior art under 35 U.S.C. § 102(a). It is requested that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 6-16 for being obvious over AC011623 in view of Maniatis *et al.* See the Office Action, page 10, lines 12-15. As discussed above, AC011623 does not qualify as prior art. Applicants submit that the rejection has been overcome.

CONCLUSION

Applicants submit that grounds for the objections and rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is useful, definite, sufficiently described, enabled, novel, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No. 08919-099001.

Respectfully submitted,

Date: 5-15-2006

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  JOURNAL   Plant Physiol. 134 (4), 1586-1597 (2004)
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  TITLE     Cloning and characterization of cDNAs for tubby-like protein 9
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  TITLE     Direct Submission
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